

Exhibit A

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In re Application of
Krishan L. Taneja
Serial No. : 09/627,796
Filed : 28 July 2000
Attorney Dkt No. : BP9806US-CP2

APPLIED BIOSYSTEMS

Decision on Petition

This letter is in response to the Request for Reconsideration under 37 C.F.R. 1.144 or 1.181 filed on 10 June 2005, to request reconsideration of the petition decision mailed 12 April 2005 for withdrawal of the restriction requirement.

BACKGROUND

A review of the file history has been summarized in the petition decision mailed 12 April 2005. On 27 April 2005 a non-final action was mailed. This request for reconsideration was filed on 10 June 2005. On 28 July 2005, applicant filed a response to the Office action.

DISCUSSION

Applicants' now request reconsideration under 37 C.F.R. 1.144 or 1.181, to withdraw the restriction requirement.

(a) Applicants correctly point out that the restriction requirement is based upon 35 USC 121.

(b) Applicants request clarification as to the Reasons for supporting the restriction requirement. The requirement for restriction under 35 USC 121 set forth on pages 5-6 of the Office action dated 21 September 2001 and summarized on page 2 of the renewed petition. Reasons provided for distinction include structural differences, functional differences and patentable distinction which followed the guidance of MPEP § 803, 806.05 - § 806.05(i).

(c) Applicants are correct that the Office must follow statute and judicial precedent.

(d) Applicants point to *In re Weber*, 580 F.2d 455, 459, 198 USPQ 328 (CCPA 1978) to argue that the restriction requirement was improper.

It is noted that *In re Weber* holds that a rejection of a single claim under 35 USC 121 is improper. Because no claim in this application has been rejected under 35 USC 121, the argument that the Office's actions are inconsistent with the holding in *In re Weber* is not persuasive.

(e) Applicants state that the decision's arguments relying upon MPRP 803.02 are off point and irrelevant.

Applicants point to a section of *In re Harnisch*, 631 F.2d 716, 722, 206 USPQ 300 (CCCPA 1980).

"It should also be clear from what we have said that we adhere to our holdings in In re Weber, supra, and In re Haas (Haas II), supra. Nothing we have said herein is intended to change or modify them in any way; nor do we think anything said could be reasonably construed to have such an effect. The "unity of invention" concept is not to be confused with the "misjoinder under 35 U.S.C. § 121" rejection employed in In re Weber. In Weber we dealt with the use of 35 U.S.C. § 121, which deals with restriction requirements to support the rejection of a single claim. Here we are concerned with the rejection of a single claim on the distinct ground that it is directed to an "improper Markush group"." (Emphasis added)

The section relied upon above from *In re Harnisch* is concerned with the rejection of a claim for containing an improper Markush group. Because no claim in this application has been rejected for containing an improper Markush group, the argument the Office's actions are inconsistent with the holding of *In re Harnisch* is not persuasive.

(f) The petition argues that restriction requirement would still be improper even if based upon "Improper Markush Grouping." This argument has two subparts.

(i) in view of 803.02, reproduced in part, below.

Since the decisions in *In re Weber*, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and *In re Haas*, 580 F.2d 461, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention. *In re Harnisch*, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility.

This subsection deals with Markush-type generic claims which include a plurality of alternatively usable substances or members. In most cases, a recitation

by enumeration is used because there is no appropriate or true generic language. A Markush-type claim can include independent and distinct inventions. This is true where two or more of the members are so unrelated and diverse that a prior art reference anticipating the claim with respect to one of the members would not render the claim obvious under 35 U.S.C. 103 with respect to the other member(s). In applications containing claims of that nature, the examiner may require a provisional election of a single species prior to examination on the merits. The provisional election will be given effect in the event that the Markush-type claim should be found not allowable. Following election, the Markush-type claim will be examined fully with respect to the elected species and further to the extent necessary to determine patentability.

(ii) Understanding and applying *Harnisch*

Applicants also point to *In re Harnisch* and MPEP 2173.05(h) to argue that the proper test for whether SEQ ID NOs 1-159 are distinct is whether they share a common utility. Applicants state that the PNA probes are all useful for detecting human chromosomes.

Before addressing the concerns (b), (d), (e) and (f) of the renewed petition, it is noted that claim 1 drawn to individual probes is set forth on the last 6 pages of this petition decision as the independent claim under examination. Applicants also claims sets of probes. The election was made for probes having SEQ ID Nos 10-16 which hybridize to Chromosome Y.

As set forth in the previous decision, with respect to the nature of the invention, the claimed probes are not traditional nucleic acids, they are PNA or Peptide-Nucleic acids and have been claimed as "Non nucleic acid probes." The difference with a PNA is that the backbone is not a traditional sugar-phosphate nucleic acid backbone, but one that has peptide structures. PNA's function like nucleic acids in that they contain a sequence of bases (usually traditional nucleotide bases) (what is termed in the claims as a probing nucleobase sequence) which is responsible for the hybridization of a PNA to DNA. Thus it is actually the nucleobase sequence that controls the function and specificity of these PNAs.

Claim 1 recites 159 sequences listed in the alternative. Representative SEQ ID NOs 1, 2 and 3 are shown below. No significant similarity is evidenced from a comparison of these three sequences. SEQ ID Nos 4-159 also appear to be unrelated, one to another, with respect to sequence similarity.

<400> 1

cttcaagag gtccacga

<400> 2
agggttcaac tgtgtgac

<400> 3
gaaacttctg agtgatga

As explained in the previous decision, the 159 peptide nucleic acid sequences recited in claim 1 of the instant application do not appear to share a common utility nor do they share any substantial structural feature, let alone any substantial feature disclosed as being essential to that utility. Probes which bind to a common structure, such as a selected chromosome, are not required to share a common structure. This is supported by the comparisons of SEQ ID Nos 10-16, which appear to share no significant structure in common and yet hybridize to Chromosome Y. This is because the probes hybridize to different regions of Chromosome Y. This is the case in the instant application and the Office has grouped the probes based on their specific chromosome binding affinity (i.e. binding to chromosomes X, Y, 1, 2, 3, 4, 6, 7, 8, 9, 10, 11, 12, 16, 17, 18 or 20, etc...) and thus every invention has been placed within a group which has a common utility.

MPEP 2175.03(h) states in part that:

The materials set forth in the Markush group ordinarily must belong to a recognized physical or chemical class or to an art-recognized class. However, when the Markush group occurs in a claim reciting a process or a combination (not a single compound), it is sufficient if the members of the group are disclosed in the specification to possess at least one property in common which is mainly responsible for their function in the claimed relationship, and it is clear from their very nature or from the prior art that all of them possess this property.

For process and combination claims, the Markush group may include members which share a common property mainly responsible for their function in the claimed relationship. It is not clear from the comparison of SEQ ID NOs 1, 2 and 3, what property, is any, that they share which is mainly responsible for their function.

Moreover, on pages 21-24 of the specification, the Table illustrates that the probes are specific for different chromosomes. Thus, SEQ ID NO: 10 which may be used to detect Chromosome Y would not be interchangeable with SEQ ID NO: 9 which may be used to detect Chromosome X. The specification discloses that each probe 1-152 cannot be substituted one for another to obtain the same effect. The specification discloses that probes 153-159 are specific for two chromosomes 13/21, however this invention was not elected for examination. Furthermore, it is not clear from the prior art or from their nature that all of the probes possess a property responsible for their function. For

example, it is not clear what common sequence shared by all of SEQ ID Nos 10-16 imparts the utility of binding to Chromosome Y.

Applicant further argues that the probes have common utility. From page 8 of the renewed petition:

That common utility was also demonstrated by the Examples and illustrated in the Figures. For Example, Figures 12A and 12B illustrate the simultaneous determination of chromosomes X, Y and 1. Thus, it is remarkable that The Office could conclude that there is no common utility for these probes where the specification so clearly demonstrates the common utility.

The Brief Description of the Drawings for Figure 12 is set forth below.

- 10 In Figure 12A and 12B the composite digital image was obtained with each of the blue, green, red (pseudo colored orange) and Cy5 (pseudocolored red) filters of a CCD camera attached to a microscope. Chromosomes X, Y and 1 are clearly detectable in the visible interphase nuclei and metaphase spreads. The cells observed in Figure 12A are from a normal human female (XX,11) and the cells observed in Figure 12B are from a normal human male (XY,11).

From the disclosure, it appears that 3 probes are used together to detect Chromosome X, Y and 11. A combination of probes specific for Chromosome X, Y and 11 are expected to detect a combination of chromosomes X, Y and 11, but this imparts a common utility among the 3 probes specific for X, Y or 11. It is not clear whether applicant is arguing that an individual probe for Chromosome X would also specifically bind chromosome Y and 11. Table 1 does not disclose any individual probe which binds chromosome X, Y and 11.

MPEP 808 sets forth further guidance for insisting upon restriction:

Every requirement to restrict has two aspects: (A) the reasons (as distinguished from the mere statement of conclusion) why the inventions *as claimed* are either independent or distinct; and (B) the reasons for insisting upon restriction there between as set forth in the following sections.

The arguments appear to be directed to the elected invention, probes comprising SEQ ID NOs 10-16. These arguments are not commensurate with the invention *as claimed*. MPEP 808 explains that it is the invention, *as claimed*, which is considered for distinctness or independence. It is noted that the invention *as claimed* does not require all SEQ ID NO 10-16. Claim 1 encompasses individual probes and sets of probes which

do not require all of SEQ ID NOs 1-159. For these reasons, the arguments are not persuasive.

MPEP 803.04 explains how claims directed to polynucleotide sequences claimed both individually and in sets will be restricted and examined. The instant claims recite both individual sequences (Example A: a probe comprising SEQ ID No 1), sets (Example B: a probe comprising SEQ ID NOs 1 and 2) and ranges of sets (Example C: a probe comprising any two selected from the group consisting of SEQ ID NOs 1-159, which reads upon using SEQ ID NOs 1 and 3, SEQ ID NOs 1 and 5, SEQ ID NOs 1-23 inclusive, etc.) MPEP 803.04 states that after restriction,

Based upon the finding of allowable sequences, claims limited to the allowable sequences as in example (A), all combinations, such as in examples (B) and (C), containing the allowable sequences and any patentably indistinct sequences will be rejoined and allowed.

Rejoinder will be permitted for claims requiring any allowable sequence(s). Any claims which have been restricted and nonselected and which are limited to the allowable sequence(s) will be rejoined and examined.

Applicants have elected PNA probes SEQ ID NOs 10-16. Applicants may also pursue generic linking claims which encompass all the features of the elected invention and should any of those become allowable, applicant may be entitled to rejoinder under MPEP 809 of any claims which require all the features of an allowable linking claim. For the instant invention, a linking claim may be drafted in the format of Claim 1, in which the list of alternative sequences in claim 1(a) is deleted and replaced with text in the format of "a probing nucleobase that hybridizes to chromosome Y."

Additionally, upon indication of an allowable claim, applicants may include claims which require all the features of the allowable inventions. If probes comprising SEQ ID Nos 10-16 are indicated as allowable, claims for any probe combinations that require SEQ ID Nos 10-16 would be considered for rejoinder as requiring all the limitations of an allowable claim. Those additional probes may be specific for additional chromosomes. But at this time no claim is of proper format for allowability in view of the rejections under 35 USC 112 and the objection for encompassing non-elected subject matter in the alternative.

DECISION

For these reasons, the Renewed Petition under 37 C.F.R. 1.144 and 1.181 to request withdrawal of the restriction requirement is **DENIED**.

The application will be forwarded to the examiner to consider the response filed 28 July 2005.

Any request for consideration must be filed within two (2) months of the mailing date of this decision.

(10/20/05)

Should there be any questions regarding this decision, please contact Special Program Examiner Julie Burke, by mail addressed to Director, Technology Center 1600, PO BOX 1450, ALEXANDRIA, VA 22313-1450, or by telephone at (571) 272-1600 or by Official Fax at 571-273-8300.



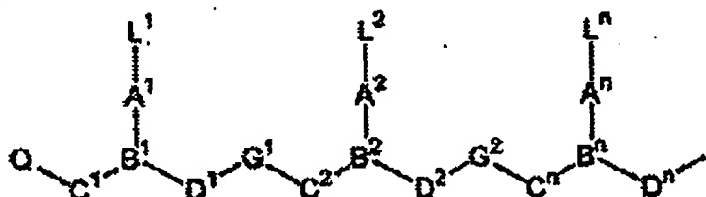
Jasmine Chambers
Director, Technology Center 1600

1. (Previously Amended) A PNA probe of up to 30 subunits in length comprising a probing nucleobase sequence selected from the group consisting of: CTT-CAA-AGA-GGT-CCA-CGA (Seq. ID No. 1); AGC-GTT-CAA-CTG-TGT-GAC (Seq. ID No. 2); GAA-ACT-TCT-GAG-TGA-TGA (Seq. ID No. 3); CAG-TCA-TCC-CAG-AAA-ACT (Seq. ID No. 4); AGA-TTT-CAC-TGG-AAA-CGG (Seq. ID No. 5); GTT-ATG-GGA-AGG-TGA-TCC (Seq. ID No. 6); TCG-AGC-CCG-AGA-GTT-TAA (Seq. ID No. 7); CTA-TTT-AGC-GGG-CIT-GGA (Seq. ID No. 8); TAC-AAG-CCT-GTT-GCA-AAC (Seq. ID No. 9); CCA-TAT-GCA-GTT-ATA-AGT-AGG (Seq. ID No. 10); TAT-TGT-ACC-AAG-CAG-AGT-ACC (Seq. ID No. 11); GGT-ATA-TAT-AAG-ATG-ACA-CAG-GA (Seq. ID No. 12); GTT-AGT-TAT-ATT-GGG-TGA-TAT-GT (Seq. ID No. 13); TCA-CAT-AAT-AGA-CAA-CAT-AC (Seq. ID No. 14); CAG-AAG-AGA-TTG-AAC-CIT (Seq. ID No. 15); GGC-ATA-GCA-CAT-AAG-ATG (Seq. ID No. 16); AAT-CGT-CAT-CCA-ATG-AAT (Seq. ID No. 17); CAT-TGA-ACA-GAA-TTG-AAT (Seq. ID No. 18); GTT-TTC-AGG-GGA-AGA-TAT (Seq. ID No. 19); TGT-GCG-CGC-TCA-ACT-AAC (Seq. ID No. 20); GAA-GCT-TCA-TTG-GGA-TGT (Seq. ID No. 21); CCA-ATA-AAA-GCT-ACA-TAG-A (Seq. ID No. 22); GAA-AAA-GTT-TCT-GAC-ATT-GC (Seq. ID No. 23); TAG-TTG-AAG-GCC-ACA-TCA (Seq. ID No. 24); CAC-AAA-TAA-GAT-TCT-AAG-AAT (Seq. ID No. 25); TCA-AAA-GAA-TGC-TTC-AAC-AC (Seq. ID No. 26); ATA-ATT-AGA-CCG-GAA-TCA-T (Seq. ID No. 27); GCT-GTT-TTC-TAA-AGG-AAA-G (Seq. ID No. 28); AAG-ACT-TCA-AAG-AGG-TCC (Seq. ID No. 29); TTT-GTC-AAG-AAT-TAT-AAG-AAG (Seq. ID No. 30); CAA-GAT-TGC-TTT-TAA-TGG (Seq. ID No. 31); TGT-GTA-TCA-ACT-CAC-GGA (Seq. ID No. 32); CCT-CAC-AAA-GTA-GAA-ACT (Seq. ID No. 33); GAA-AAA-GCA-GTT-ACT-GAG (Seq. ID No. 34); TAA-TAA-TTA-GAC-GGA-ATC-AT (Seq. ID No. 35); TTA-CAG-GCC-ATT-GAA-GCC (Seq. ID No. 36); CAG-TTA-TGA-
-

AGC-AGT-CTC (Seq. ID No. 37); CAC-ACC-AGA-AAA-AGC-AGT (Seq. ID No. 38); AAG-GGT-AAA-CAC-TGT-GAG (Seq. ID No. 39); AGA-CAA-CGA-AAT-ATC-TTC-ATG (Seq. ID No. 40); CTA-GCA-GTA-TGA-GGT-CAA (Seq. ID No. 41); GCA-GAC-TTC-AGA-AAC-AGA (Seq. ID No. 42); GGC-CTC-AAA-GAC-GTT-TAA (Seq. ID No. 43); CTC-AAA-GTT-CCA-AGT-GAA (Seq. ID No. 44); GAG-TCC-TTT-GAA-GCC-TAC (Seq. ID No. 45); GAA-ACA-GCA-GAG-TTG-AAA (Seq. ID No. 46); TGC-AGA-GAT-CAC-AAC-GTG (Seq. ID No. 47); ACA-AAG-AAT-CAT-TCC-CAG (Seq. ID No. 48); AGT-GTT-AGA-AAA-CTG-CTC (Seq. ID No. 49); ACA-GGA-TTT-TGC-AAA-CAC (Seq. ID No. 119); CGA-AAG-ATC-ACT-GAG-AGT (Seq. ID No. 120); GGA-TGA-CAT-ATA-ATA-ACT-AG (Seq. ID No. 121); GAA-TTG-AAC-ATT-CAC-TTT-GA (Seq. ID No. 122); TAG-CTC-TGA-AGA-TTT-CGT (Seq. ID No. 123); GAG-ATG-TTT-CCG-AGA-ATG (Seq. ID No. 124); GTG-TTT-TCA-ACT-ACC-AGA (Seq. ID No. 125); ACA-TTT-CTG-TTA-CAG-AGC (Seq. ID No. 126); ATG-ACG-TAT-AAA-ATC-TAG-AG (Seq. ID No. 127); ACG-AAC-ACA-GTT-GAA-CCT (Seq. ID No. 128); CTC-ATA-AAA-ACC-AGA-AAG-AG (Seq. ID No. 129); CTG-TTC-AGA-GTA-ACA-TGA (Seq. ID No. 50); CCC-CTT-GGA-AAT-ACT-ACA (Seq. ID No. 51); GAA-ATG-GAA-ATA-TCT-CCC-C (Seq. ID No. 52); TCT-AGG-ACG-TCC-AAT-TAT (Seq. ID No. 53); GAA-TTC-CCA-AGT-GGA-TAT (Seq. ID No. 54); CTG-TAG-GTT-TAG-ATG-AAG (Seq. ID No. 55); AAG-GAG-TGT-TTC-CCA-ACT (Seq. ID No. 56); GGC-TTC-AAG-GCG-CTC-TAA (Seq. ID No. 57); GCA-GAG-ACT-TCA-AAG-TGC (Seq. ID No. 58); CAC-ACA-CAC-GGT-GGA-CCA (Seq. ID No. 59); CAA-AGG-GAA-TGT-TCC-ATT (Seq. ID No. 60); CAC-ATA-GCA-CTG-TTT-GAG (Seq. ID No. 61); CTC-AAG-GCG-GTC-CAA-TTA (Seq. ID No. 62); GAG-TCG-AAA-TGC-ACA-CAT (Seq. ID No. 63); TAC-CAA-GAG-GAA-TGT-TGC (Seq. ID No. 64); CAG-TTC-ATA-TGT-GCA-GTG (Seq. ID No. 130); GGA-ATA-TCG-TCA-CCT-AAA (Seq. ID No. 131); TGC-AGC-AAA-TTG-AAG-CCT (Seq. ID No. 132); TGG-AGC-ACA-TTT-ATG-CCT (Seq. ID No. 133); TGC-ATT-CTA-CTC-CCA-TAG (Seq. ID No. 134); ACA-CTC-TGT-TTC-TAA-AAT-CT (Seq. ID No. 135); GCA-GGC-GGA-TAT-TTA-GTA (Seq. ID No. 136); AGC-GAT-TTG-ATG-CCA-ACA (Seq. ID No. 137); TTG-CAA-ACG-GGG-TTT-CTT (Seq. ID No. 138); CTT-TCA-TGC-TAG-ACA-GAA (Seq.

ID No. 139); CAA-AAA-AGT-TAC-TGA-GAA-C (Seq. ID No. 140); AAA-ATG-CCA-CAG-CAA-GAG (Seq. ID No. 141); GTT-TGA-AAA-CAC-ACT-GTT-TG (Seq. ID No. 142); ATA-TGG-ACC-TGT-TTG-AGG (Seq. ID No. 143); CAT-TGA-ATG-CTA-GAC-GGA (Seq. ID No. 144); ACG-GGA-TGC-AAT-ATA-AAA (Seq. ID No. 65); TGA-TGA-TTC-TGC-ATA-CCG (Seq. ID No. 66); AAG-GTT-TGT-ACT-GAC-AGA (Seq. ID No. 67); CTG-AAC-TAT-GGT-GAA-AAA (Seq. ID No. 68); ACT-AAC-TGT-GCT-GAA-CAT (Seq. ID No. 69); CCC-ATG-AAT-GCG-AGA-TAG (Seq. ID No. 70); ATG-ATG-AAA-AAG-GTA-ATA (Seq. ID No. 145); CAT-TCT-CAG-AAC-TGT-TTG (Seq. ID No. 146); AAC-TGA-ACG-CAC-AGA-TGA (Seq. ID No. 71); GGC-TAA-TCT-TTG-AAA-TTG-AAA (Seq. ID No. 72); ACG-TGG-ATA-ATT-GCC-CCT (Seq. ID No. 73); TGA-AGT-CCA-AAA-AAG-CAC (Seq. ID No. 74); CTT-AGA-CAT-GGA-AAT-ATC (Seq. ID No. 75); AAG-GGG-TCT-AAC-TAA-TCA (Seq. ID No. 76); GTA-GTT-GTT-GAG-AAT-GAT (Seq. ID No. 77); AAC-TTC-CCA-GAA-CTA-CAC (Seq. ID No. 78); ATT-CTT-GAA-ATG-GAA-CAC (Seq. ID No. 79); CTG-TGA-TTG-CTG-ATT-TGG (Seq. ID No. 80); GTC-ATC-ACA-GGA-AAC-ATT (Seq. ID No. 81); GAA-ATT-TCC-TGT-TGA-CAC-A (Seq. ID No. 82); GTT-TGA-AAG-CTG-AAC-TAT-G (Seq. ID No. 83); TCC-TGT-AAT-GTT-CCA-CAG (Seq. ID No. 84); TCA-TAG-AAC-GCT-AGA-AAG (Seq. ID No. 85); ACC-TTT-CTT-TTG-ATG-AAG-GA (Seq. ID No. 86); CAA-ATA-TCA-CAA-AAA-GAG-GG (Seq. ID No. 87); GAG-TTG-AAT-AGA-GGC-AAC (Seq. ID No. 88); GGC-CAA-ATG-TAG-AAA-AGG (Seq. ID No. 89); GCG-TTC-AAC-TCA-AGG-TGT (Seq. ID No. 90); TGT-CCT-TTA-GAC-AGA-GCA (Seq. ID No. 91); TGA-GAC-CAA-ATG-TAC-AAA-AG (Seq. ID No. 92); GAA-TAC-TGA-GTA-AGT-TCI-TTG (Seq. ID No. 93); AAC-TGC-ACA-AAT-ACG-GTG (Seq. ID No. 94); TGG-AGA-CAC-TGT-GTT-TGT (Seq. ID No. 95); CCA-GTT-GGA-GAT-TTC-AAT (Seq. ID No. 96); GAA-GCC-TGC-CAG-TGG-ATA (Seq. ID No. 97); TAC-AGC-ATT-CTG-GAA-ACC (Seq. ID No. 98); CCA-GAC-ACT-GCG-TAG-TGA (Seq. ID No. 99); ATA-TAA-TGC-TAG-AGG-GAG (Seq. ID No. 100); AAA-AAC-AAG-ACA-AAC-TCG (Seq. ID No. 101); ATT-TCA-GCT-GAC-TAA-ACA (Seq. ID No. 102); AAC-GAA-TTA-TGG-TCA-CAT (Seq. ID No. 103); GGT-GAC-GAC-TGA-GTT-TAA (Seq. ID No. 104); TTT-GGA-CCA-CTC-TGT-GCC (Seq. ID No. 105); AAC-GCG-ATA-ACT-GCA-CCT

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wherein,

n is at least 2,

each of L^1 - L^n is independently selected from the group consisting of hydrogen, hydroxy, (C_1-C_6) alkanoyl, naturally occurring nucleobases, aromatic moieties, DNA intercalators, nucleobase-binding groups, heterocyclic moieties, and reporter ligands;

each of C^1 - C^n is (CR^1R^2) , where R^1 is hydrogen and R^2 is selected from the group consisting of the side chains of naturally occurring alpha amino acids, or R^1 and R^2 are independently selected from the group consisting of hydrogen,

(C₁-C₆)alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C₁-C₆)alkoxy, (C₁-C₆)alkylthio, NR³R⁴ and SR³, where R³ and R⁴ are as defined above, and R³ is hydrogen, (C₁-C₆)alkyl, hydroxy-, alkoxy-, or alkylthio-substituted (C₁-C₆)alkyl, or R³ and R⁴ taken together complete an alicyclic or heterocyclic system;

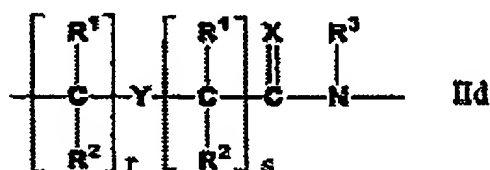
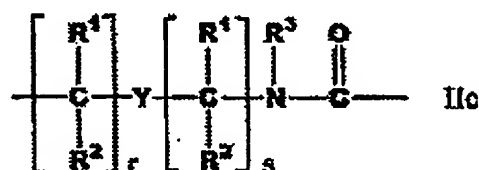
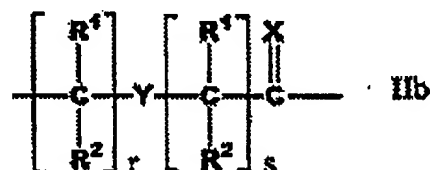
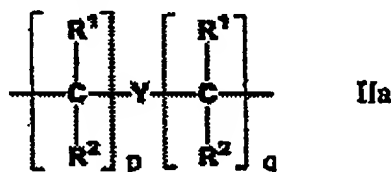
each of D¹-D³ is (CR⁵R⁶), where R⁵ and R⁶ are as defined above;

each of y and z is zero or an integer from 1 to 10, the sum y+z being greater than 2 but not more than 10;

each of G²-G⁴ is -NR³CO-, -NR³CS-, -NR³SO- or -NR³SO₂-, in either orientation, where R³ is as defined above;

each of A¹-A⁴ and B¹-B⁴ are selected such that:

- (a) A is a group of the formula (IIa), (IIb), (IIc), or (IId), and B is N or R³N⁺; or
- (b) A is a group of formula (IId) and B is CH:



where:

X is O, S, Se, NR^p, CH, or C(CH₃)₃;

Y is a single bond, O, S or NR^q;

each of p and q is zero or an integer from 1 to 5, the sum of p+q being not more than 10;

each of r and s is zero or an integer from 1 to 5, the sum of r+s being not more than 10;

each R^p and R^q is independently selected from the group consisting of hydrogen, (C₁-C₅)alkyl which may be hydroxy- or alkoxy- or alkylthio-substituted, hydroxy, alkoxy, alkylthio, amino and halogen; and

each R^r and R^s is independently selected from the group consisting of hydrogen, (C₁-C₅)alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C₁-C₅)alkyl, hydroxy, alkoxy, alkylthio and amino;

Q is -CO₂H, -CONR^r, -SO₃H or -SO₂NR^r or an activated derivative of -CO₂H or -SO₃H; and

I is -NHR^rR^s or -NR^rC(O)R^s, where R^r, R^s, R^r and R^s are independently selected from the group consisting of hydrogen, alkyl, amino protecting groups, reporter ligands, intercalators, chelators, peptides, proteins, carbohydrates, lipids and steroids.